Healthcare Improvement Scotland

SIGN
Scottish Intercollegiate Guidelines Network

Risk reduction and management of delirium

A national clinical guideline

Consultation draft, June 2018

Evidence

Key to evidence statements and recommendations

LEVELS OF EVIDENCE

1^{++}	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

RECOMMENDATIONS

Some recommendations can be made with more certainty than others. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the 'strength' of the recommendation).

The 'strength' of a recommendation takes into account the quality (level) of the evidence. Although higher-quality evidence is more likely to be associated with strong recommendations than lower-quality evidence, a particular level of quality does not automatically lead to a particular strength of recommendation.

Other factors that are taken into account when forming recommendations include: relevance to the NHS in Scotland; applicability of published evidence to the target population; consistency of the body of evidence, and the balance of benefits and harms of the options.

R For '**strong**' recommendations on interventions that '**should**' be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more good than harm. For '**strong**' recommendations on interventions that '**should not**' be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more harm than good.

R For '**conditiona**l' recommendations on interventions that should be '**considered**', the guideline development group is confident that the intervention will do more good than harm for **most** patients. The choice of intervention is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time discussing the options with the patient, where possible.

GOOD-PRACTICE POINTS

✓ Recommended best practice based on the clinical experience of the guideline development group.

Contents

1 Introduction

1.1 THE NEED FOR A GUIDELINE

Delirium is a severe, acute deterioration in mental functioning arising over hours or days that is triggered mainly by acute medical illness, surgery, trauma, or drugs.[1] It was previously termed 'acute confusional state'. Delirium is independently linked with poor outcomes including medical complications, falls, increased length of hospital stay, new institutionalisation, and mortality.[1] It can cause significant patient and carer distress.

The main features of delirium are acute cognitive deficits and altered level of arousal, with up to half of patients also experiencing hallucinations or delusions.[2] Delirium varies in duration, mostly resolving within days, but in some people it can last weeks or months.[3] It can affect any individual, though old age, the presence of dementia and multiple comorbidities greatly increase vulnerability.[1]

Delirium is among the most common of medical emergencies. The prevalence in acute general medical settings is reported as 18 to 35%.[4] Prevalence is higher in particular groups, such as older patients and patients in intensive care units (ICU). In the United States figures show that one third of general medical patients over the age of 70 experience delirium, and it affects 10 to 15% of older people admitted to hospital as emergencies, 50% who have hip fracture and 75% in intensive care.[1]

Despite its importance, there are deficiencies in care of people with delirium in Scotland. It is underdiagnosed[5] and the treatment of patients with established delirium is variable. Preventative measures can reduce the incidence of delirium,[1] yet few clinical units have formal delirium risk reduction programmes.

Experience of quality improvement programmes in Scotland show that advances can be made.[6] There is potential to improve clinical practice by reducing variation in the standards of assessment and management of people with delirium. This new national guideline on delirium provides a critical focal point for Scotland-wide improvements on delirium care. Because delirium is so common, all healthcare staff having contact with acutely unwell patients need to assume responsibility for detecting and treating it, as well as aiming to reduce the risk of it occurring. Those working in the long-term care environment should be able to recognise delirium, reduce risk, and monitor those in their care to resolve delirium.

1.1.1 PATIENT AND CARER PERSPECTIVE

Common concerns raised by patient groups and through research into patient and carer issues identified good communication with family members or carers as crucial. Family members can provide background information on patient history, changes in behaviour and early warning signs. Once diagnosed, carers need information and support to enable them to care for the patient (*see section 9.1 sources of further information*).

1.2 REMIT OF THE GUIDELINE

1.2.1 OVERALL OBJECTIVES

This guideline provides recommendations based on current evidence for best practice in the diagnosis, management and follow up of adults with delirium across all settings (home, long-term care, hospital, and hospice).

It excludes delirium secondary to alcohol and illicit substances use, and paediatric delirium.

1.2.2 COMMON COMORBIDITIES

Common comorbidities which have been considered when reviewing the evidence for this guideline are:

- critical illness
- dementia
- depression
- frailty
- head injury
- learning disability
- Parkinson's disease
- cerebrovascular disease.

1.2.3 DEFINITIONS

ICD-10 defines delirium as, "An etiologically nonspecific organic cerebral syndrome characterized by concurrent disturbances of consciousness and attention, perception, thinking, memory, psychomotor behaviour, emotion, and the sleep-wake schedule. The duration is variable and the degree of severity ranges from mild to very severe".[7]

Delirium presents variably but its main characteristics are rapid onset (hours, days) of acute mental status deterioration. Patients may present with cognitive impairment, but drowsiness to the point that the patient is not speaking, severe agitation, or psychotic features such as hallucinations or delusions may be the most prominent features. Delirium can be described using hyperactive, hypoactive or mixed labels depending on the level of arousal, though this is not done in every case. Most delirium has a duration of a small number of days, but in around of 20% of cases, it can persist for weeks or months.[8]

Delirium is known by several terms, some still in use in clinical practice. These terms include 'acute confusional state', 'acute confusion', 'acute on chronic confusion', and 'acute encephalopathy'. The SIGN guideline group advocate use of the term delirium rather than alternatives to promote more consistent communication among professionals, more accurate provision of information to patients and carers, and more consistent use of detection tools and management strategies.

1.2.4 TARGET USERS OF THE GUIDELINE

This guideline will be of interest to primary and secondary healthcare professionals, community and care home staff involved in the care of patients at risk of, or experiencing, delirium, as well as patients and carers.

1.3 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results.

The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at through a process of shared decision making with the patient (or family or carers, where appropriate), covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be documented in the patient's medical records at the time the relevant decision is taken.

1.3.1 INFLUENCE OF FINANCIAL AND OTHER INTERESTS

It has been recognised that financial interests in, or close working relationships with, pharmaceutical companies may have an influence on the interpretation of evidence from clinical studies.

It is not possible to completely eliminate any possible bias from this source, nor even to quantify the degree of bias with any certainty. SIGN requires that all those involved in the work of guideline development should declare all financial interests, whether direct or indirect, annually for as long as they are actively working with the organisation. By being explicit about the influences to which contributors are subjected, SIGN acknowledges the risk of bias and makes it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are based on a biased interpretation of the evidence.

Signed copies of declaration of interests forms are retained by the SIGN Executive and a register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

1.3.2 PRESCRIBING OF LICENSED MEDICINES OUTWITH THEIR MARKETING AUTHORISATION

Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (MA) also known as product licence. This is known as 'off-label' use.

Medicines may be prescribed 'off label' in the following circumstances:

- for an indication not specified within the marketing authorisation
- for administration via a different route
- for administration of a different dose
- for a different patient population.

An unlicensed medicine is a medicine which does not have MA for medicinal use in humans.

Generally 'off-label' prescribing of medicines becomes necessary if the clinical need cannot be met by licensed medicines within the marketing authorisation. Such use should be supported by appropriate evidence and experience.[9]

"Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability."[9]

The General Medical Council (GMC) recommends that when prescribing a medicine 'off label', doctors should:[10]

- be satisfied that there is no suitably licensed medicine that will meet the patient's need.
- be satisfied that there is sufficient evidence or experience of using the medicine to show its safety and efficacy
- take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring, and any follow up treatment, or ensure that arrangements are made for another suitable doctor to do so the effects of the medicine.
- Make a clear, accurate and legible record of all medicines prescribed and, when not following common practice, the reasons for prescribing an unlicensed medicine.

Non-medical prescribers should ensure that they are familiar with the legislative framework and their own professional prescribing standards.

Prior to any prescribing, the licensing status of a medication should be checked in the summary of product characteristics (www.medicines.org.uk). The prescriber must be competent, operate within the professional code of ethics of their statutory bodies and the prescribing practices of their employers.[11]

1.3.3 HEALTH TECHNOLOGY ASSESSMENT ADVICE FOR NHSSCOTLAND

Specialist teams within Healthcare Improvement Scotland issue a range of advice that focuses on the safe and effective use of medicines and technologies in NHSScotland.

The Scottish Medicines Consortium (SMC) provides advice to NHS boards and their Area Drug and Therapeutics Committees about the status of all newly-licensed medicines, all new formulations of existing medicines and new indications for established products. NHSScotland should take account of this advice and ensure that medicines accepted for use are made available to meet clinical need where appropriate.

SMC advice relevant to this guideline is summarised in the section on implementation.

2 Key recommendations

The following recommendations were highlighted by the guideline development group as the key clinical recommendations that should be prioritised for implementation.

2.1 DETECTING DELIRIUM

R **The 4AT tool should be used for identifying patients at higher risk of delirium in emergency and acute hospital settings.**

✓ Where delirium is detected, the diagnosis of delirium should be clearly documented and coded for transfers of care (eg handover notes, referral and discharge letters).

2.2 RISK REDUCTION

R **The following components should be considered as part of a package of care for patients at risk of developing delirium:**

- **orientation**
- **early mobilisation**
- **pain control**
- **prevention, early identification and treatment of postoperative complications**
- **maintaining optimal hydration and nutrition**
- **regulation of bladder and bowel function**
- **provision of oxygen, if required.**

R **All patients with delirium should have a medication review conducted by an experienced healthcare professional.**

2.3 NON PHARMACOLOGICAL TREATMENT

R **Healthcare professionals should follow established pathways of good care to manage patients with delirium:**

- **First consider acute, life-threatening causes of delirium, including low oxygen, low blood pressure, low glucose, and drug intoxication.**
- **Systematically identify and treat potential causes** (drug, acute illness, etc)**, noting that multiple causes are common.**
- **Optimise physiology, management of concurrent conditions, environment** (reduce noise)**, medications, and natural sleep, to promote brain recovery.**
- **Specifically detect, assess causes of, and treat agitation and/or distress, using non-pharmacological means only if possible.** *(See section 7 for pharmacological treatment).*
- **Communicate the diagnosis to patients and carers, and provide ongoing engagement and support.**
- **Aim to prevent complications of delirium such as immobility, falls pressure sores, dehydration, malnourishment, isolation.**
- **Monitor for recovery and consider specialist referral if not recovering.**
- **Consider follow-up** (*see section 8*).

3 Detecting delirium

3.1 TOOLS FOR DETECTION AND ASSESSMENT

Delirium is frequently missed in routine clinical care and lack of detection is associated with poor outcomes.[12,13] Numerous assessment tools have been developed to help identify probable delirium in patients in a variety of settings, which then prompts a more accurate diagnosis and consideration of underlying causes. For practical reasons for implementation and acceptability to patients, assessment tools should be brief, require little or no training and be appropriate to the clinical setting.[14] The sensitivity of the tool is also important, as it is a priority not to miss delirium.

A commonly used tool, the Confusion Assessment Method (CAM) and its variants have been reported as useful tools for detecting delirium.[12,15,16] However, sensitivities and specificity varied broadly, possibly due to the need for users to have training and knowledge of delirium and its differential diagnoses. The CAM-ICU has particularly broad use within ICU settings but has the same limitations.[13,17] In non-ICU settings the 4 A's Test (4AT) was developed, validated and widely implemented in Scotland. It does not require specific training, is brief and easy to use and has wide applicability in various clinical settings.[18,19] Therefore some studies have recommended the 4AT over CAM as it is less open to interpretation and quicker to use.[14,20] The 4AT is also supported as the assessment tool of choice in older emergency department attendees.[21]

2+
2++
2+

Other tools had significant disadvantages over CAM and 4AT, such as longer assessment time, poorer sensitivity and/or specificity, and/or relative lack of validation (*see Table 1: Overview of delirium assessment tools*). The 13-item Delirium Observation Screening Scale (DOS) had good specificity and sensitivity but requires assessment over three shift periods and its authors have suggested it is geared more towards detection of hyperactive delirium, whereas hypoactive is more common in practice.[22-24]

2+
2++

The CAM-ICU and Intensive Care Delirium Screening Checklist (ICDSC) have been developed and validated in ICU settings, and may be better suited than other tests for use in intensive care.[25]

2+

In all cases, a positive assessment should be followed by additional assessment and diagnosis against DSM-5 criteria by a suitably trained clinician. Note that delirium may still occur in the absence of a positive test result because the condition fluctuates. Healthcare staff should not rely on the result of a single assessment during hospital admission.

Assessment of the patient's capacity to make decisions about fundamental health and personal care should also be taken into consideration. If the person is deemed to be incapacitated appropriate documentation (Adults with Incapacity Act, Section 47 part 5 certificate with accompanying treatment plan) should be completed.

Table 1 summarises the commonly used and validated brief delirium assessment tools. There is a wide range of sensitivities and specificities with the different tools as well as the time taken to complete assessment. A tool with high sensitivity that requires no training or very little time to perform and with additional advantages (example, suitable for patients with dementia) will be important in clinical practice to ensure all cases of delirium are identified. In the case of confusion whether there is delirium or dementia or both it is best to assume it is delirium unless there is indication from the patient's notes or from family members that the mental state is clearly in keeping with the baseline.

Table 1: Overview of delirium assessment tools

Tool	Time taken (min)	Training Required	Staff	Settings	Sensitivity %	Specificity %	Delirium severity rating	Suitable for monitoring	Suitable for detecting DSD	Study quality
4AT[14,18,20,24,26]	<2	No	Any	Multiple	86-100	65-82	No	No	Yes	2++, 2+
AMT[14,20]	2	No	Any	Medical	75-87	61-64	No	No	No	2++
CAM and variants[12,14,16,18,24]	3 to 10	Yes	Any	Multiple	46-94	63-100	No	No	No	2+, 2++
CAM-ICU[13,16,24,25]	<5	Yes	Any	ICU	28-100	53-99	No	Yes	No	2+
DOS (13-item)*[22-24]	5	Minimal	Any	Multiple	89-100	87-97	Yes	Yes	No	2+, 2++
DRS-98-R[24,27,28]	20	Yes	Psychiatry	Multiple	57-93	82-98	Yes	No	Yes	2+
ICDSC[13,25]	7-10	Minimal	Any	ICU	73-97	69-97	Yes	No	No	2+
MMSE[29]	5	Minimal	Any	Multiple	76-91	51-84	Yes	No	No	2+
Nu-DESC[24]	<5	No	Any	Multiple	32-96	69-92	No	No	No	2+
RASS/mRASS[30]	1	No	Any	Multiple	65-75	82-90	Yes	Yes	Yes	2++
RADAR[31]	<1	No	Any	Multiple	43-84	64-78	No	Yes	No	2++
SQiD[14]	<1	No	Any	Medical	77-91	56-71	No	No	No	2++

Suitability for monitoring refers to the use of a tool daily or more for screening for incident delirium.

*DOS requires assessment over three shifts so time to detection is three days. It is geared towards assessment of hyperactive delirium.

Abbreviations: AMT – Abbreviated Mental Test; CAM – Confusion Assessment Method; DSD – delirium superimposed on dementia; DRS-98-R – Delirium Rating Scale; DOS - Delirium Observation Screening Scale; ICDSC – Intensive Care Delirium Screening Checklist; Nu-DESC – Nursing Delirium Scale; MMSE – Mini Mental State Examination; RADAR – Recognising acute delirium as part of your routine; RASS – Richmond Agitation-Sedation Scale; SQiD – Single Question to Identify Delirium

R **The 4AT tool should be used for identifying patients at higher risk of delirium in emergency and acute hospital settings.**

R **For intensive care unit settings, CAM-ICU or ICDSC should be considered to help identify delirium.**

✓ Where delirium is detected, the diagnosis of delirium should be clearly documented for transfers of care (eg handover notes, referral and discharge letters).

3.2 CLINICAL INVESTIGATIONS

Many conditions can trigger delirium. There is often more than one contributor in an individual person.[32] A major part of treating people with delirium is treating the underlying precipitants or causes. A structured approach should be taken to identify, where possible, the issues contributing to delirium for an individual (*see Annex 2*). These include a good history from the person, a collateral or informant history, clinical examination (including a neurological examination), basic and then targeted investigations.

There is little evidence base supporting the use of basic investigations because a basic standard of care is assumed in trials, and trials do not exist comparing the testing versus not testing of, for example, a full blood count in a person with delirium.

This section examines the available evidence for advanced investigations which are more invasive or expensive where a condition may be identified which significantly alters the management of a person (eg identifying stroke, subdural haemorrhage or non-convulsive status epilepticus).

Strategies for such an approach and systems of care provide this, are outlined in the the Royal College of Physicians' 'Acute Care Toolkit 3: Acute medical care for frail older people' and in the Healthcare Improvement Scotland TIME Bundle (*see Annex 3*).[33]

3.2.1 BRAIN IMAGING

The aim of brain imaging is to identify stroke, haemorrhage or trauma as causes of delirium. The diagnostic yield of computed tomography (CT) in determining the cause of delirium is low, but may be indicated in some high-risk patients.[34] For patients with pre-existing cognitive impairment who have other identified conditions that can precipitate delirium, such as dehydration or infection, brain imaging is unlikely to change management.[35] 3

Observational, mostly retrospective, studies identified abnormal brain imaging in CT scans in people aged over 70 years presenting with acute confusion and:

- new focal neurological signs[35-39] (defined as acute onset dysphasia, visual field defect, pyramidal or cerebellar signs.[37] There should be awareness that dysphasia (a focal sign) may be mistaken as confusion (a global brain dysfunction)[40] 3 4
- presenting after a fall[37,39]
- a reduced level of consciousness (Glasgow Coma Score <9)[37,38]
- a head injury (in patients of any age)[41]
- taking anticoagulant therapy.[39]

Cerebral atrophy is more likely in patients presenting with delirium than without.[42] This in itself, however, is not a useful finding in making a diagnosis of delirium or changing medical management. 3

R CT brain should not be used routinely but should be considered in patients presenting to hospital with delirium in the presence of:

- new focal neurological signs
- a reduced level of consciousness (not adequately explained by another cause)
- a history of recent falls
- a head injury (patients of any age)
- anticoagulation therapy.

✓ Consideration should be given to scanning patients with non-resolving delirium where no clear cause is identified or there are features to suggest primary central nervous system pathology.

3.2.2 ELECTROENCEPHALOGRAM

Currently electroencephalogram (EEG) is not performed routinely in patients with delirium, however, three retrospective studies from an epilepsy research group suggest that the incidence of epileptic activity and non-convulsive status epilepticus (NCSE) are higher than recognised in patients with delirium. One study found that 80% of patients with NCSE had delirium attributed to another cause initially.[43] 3

Continuous EEG monitoring is more sensitive than single EEG assessment at identifying epileptic activities and NCSE (28% vs 6%).[43] 3

One study found that EEG can aid differentiation between patients with dementia and patients with dementia and delirium.[44] 3

EEG using a small number of leads may be helpful in identifying patients with or without delirium in a cardiothoracic ICU setting. Use of a minimal lead set aided the practicality of performing the EEG examination.[45] 3

Further evidence is needed to determine the efficacy of routine use of EEG in patients presenting with confusion.

R **Electroencephalogram should be considered when there is a suspicion of epileptic activity or non convulsive status epilepticus as a cause of a patient's delirium.**

3.2.3 LUMBAR PUNCTURE

Only one small study from the 1980s was identified on the use of lumbar puncture in the assessment of patients with delirium. It concluded that most patients with fever and delirium have a cause other than infection in the central nervous system (80 of 81 samples were negative for bacterial growth). Given the age of the trial viral polymerase chain reaction (PCR) testing is unlikely to have been performed.[46] 3

Lumbar puncture is not a straightforward procedure and such an invasive investigation may cause further distress to someone who may be confused or agitated. There is also a risk of adverse events, such as infection, causing spinal haematoma, cerebrospinal fluid (CSF) leak or low pressure CSF headache.[47]

✓ Lumbar puncture should not be performed *routinely* on patients presenting with delirium.

3.3 MONITORING

Monitoring patients diagnosed with delirium for changes in severity or response to treatment may help predict the full clinical impact.[48,49] Insufficient evidence was identified to recommend a particular tool for monitoring purposes, however, selection of a tool should take into consideration time required and ease of use.

3

Table 1 in section 3.1 lists tools that assess severity and out of these the RADAR, 13 item DOS, RASS/mRASS, CAM-ICU and ICSDC can be considered as tools for monitoring purposes in suitable clinical areas.

4 Non-pharmacological risk reduction

4.1 INTRODUCTION

Delirium is often multifactorial. Prevention may merge with treatment for non-pharmacological practices. Risk reduction should therefore be considered throughout the patient's care. Many of the acute factors triggering delirium or lowering the threshold of risk are modifiable. Targeting these modifiable factors forms the basis of reducing the risk of delirium. Up to 50% of delirium in hospitalised patients arises after hospital admission.[1,50] Categories of risk reduction include preventing physiological derangements such as dehydration and hypoxia, maintaining sleep, reducing psychological stress through communication and managing the environment, and correcting sensory impairments when possible. These non-pharmacological strategies have often been delivered in multicomponent packages, and trials of such packages form the majority of the evidence. Because of limited resources, targeting of higher risk patients (eg older people, or those with cognitive impairments) for specific delirium risk reduction strategies is commonly advocated.[51,52] To date, these strategies are considered distinct from the use of drugs to reduce the risk of delirium (*see section 5*), and are advocated in expert opinion pathways and guidelines.[52-54]

Non-pharmacological practices should be tried first before pharmacological interventions are considered.

4.2 INPATIENT CARE

Studies in a variety of patients and settings (acute and peri-operative) have found multicomponent interventions to be effective in reducing incidence of delirium.[55-58] Meta-analysis of seven studies found that compared to usual care there was a significant reduction in incidence of delirium with multicomponent interventions, with a relative risk (RR) of 0.73, 95% confidence interval (CI) 0.63 to 0.85.[56] Pooled analysis in a Cochrane Review also reported a reduction in incidence of delirium, (RR) 0.69, 95% CI 0.59 to 0.81 compared to usual care.[57] Interventions included in multicomponent care varied, but consisted of some of the following; physiotherapy, reorientation, early mobilisation, identification and treatment of underlying causes or postoperative complications, pain control, regulation of bowel and bladder function, hydration and nutrition, and oxygen delivery.[55-57] Such interventions are considered to be good basic care.[57] Comprehensive geriatric care, defined as a specialist geriatric orthopaedics team providing comprehensive medical assessment, management and initiation of rehabilitation, was also associated with lower incidence of delirium during the hospital stay and at one month.[59] Most of the studies identified in the systematic reviews were medium or low quality.	2++ 1++ 1+
Use of a checklist may help to embed good basic care and reduce incidence of delirium in postoperative patients.[56,57,60] Educating relatives or carers to deliver non-pharmacological multicomponent interventions, such as reorientation, can also reduce the incidence of delirium. One randomised controlled trial (RCT) reported an 8% reduction in the incidence of delirium in those patients cared for by relatives who were educated in delivering a re-orientating intervention versus care as usual, RR 0.42, 95% CI 0.19 to 0.92.[55]	1+ 1++ 2++

Expert consensus recommends the use of multicomponent interventions as basic good practice.[52,61,62] Pathways for good practice for risk reduction and management are in Annexes 3 and 4. | 4

R **The following components should be considered as part of a package of care for patients at risk of developing delirium:**

- **orientation**
- **early mobilisation**
- **pain control**
- **prevention, early identification and treatment of postoperative complications**
- **maintaining optimal hydration and nutrition**
- **regulation of bladder and bowel function**
- **provision of oxygen, if required.**

4.2.1 ANAESTHETIC MANAGEMENT

Using monitoring to avoid episodes of deep anaesthesia in patients aged over 60 under general anaesthesia for surgery lasting more than one hour can significantly reduce the risk of developing postoperative delirium. Two RCTs have shown reductions of 16.7% in the monitoring group versus 21.4% in the control group[63] and 15.6% intervention versus 24.1% control.[64] A substudy from a large RCT showed a reduction that did not reach statistical significance (18.8% in the intervention group and 28.0% in the control group), however, meta-analysis of the three trials and one further study of bispectral index-guided sedation reported an odds ratio (OR) of 0.56, 95% CI 0.42-0.73.[65] None of the studies included patients with dementia, emergency anaesthesia or surgery for hip fracture in older patients. | 1++ 1+

R **Depth of anaesthesia monitoring should be used in all patients aged over 60 years under general anaesthesia for surgery expected to last for more than one hour, with an aim of avoiding excessively deep anaesthesia.**

4.3 INTENSIVE CARE

A number of studies of non-pharmacological interventions in ICU settings were identified.[66-71] Interventions included acupuncture, mirror therapies, and range of motion exercises. Most of the studies were underpowered. The largest trial addressed the use of dynamic light therapy to reduce the incidence and duration of delirium in patients in ICU.[71] It did not find the therapy to be more effective than placebo. Due to the heterogeneity of interventions and populations no single intervention for patients in ICU can be recommended. | 1+ 1-

A systematic review of eight studies of a multicomponent care approach reported benefit in five of the studies.[72] The other three studies showed no difference between the treatment and control groups. However, the multicomponent care approach is considered as standard good practice (*see section 4.2*), and the effect of multi-modal therapy may not be as evident as in other patient groups, given that critically ill patients exhibit ongoing risk factors for much of their critical care admission. | **1+**

The use of earplugs, either alone or along with eye shades and other noise reducing strategies to promote sleep in ICUs, was associated with a reduction in incidence of delirium, RR 0.59, 95% CI 0.44 to 0.78, in a systematic review of five low-quality studies (832 patients).[73] Suitability for earplugs should be considered on an individual basis as there may be a risk of exacerbating confusion in some patients. | 2++

R **The use of earplugs should be considered as part of a sleep promotion strategy in intensive care.**

5 Pharmacological risk reduction

5.1 MEDICINES OPTIMISATION

Delirium has numerous causes that interact in any one person to cause delirium. Several classes of medication can increase the likelihood of delirium occurring, and the probability of a drug to precipitate delirium should be considered when prescribing, particularly in those at increased risk of delirium.[55,74,75] Observational evidence suggests that exposure to certain drugs increases the odds of delirium developing and that medication review can decrease rates of delirium.[74-77] The following is an approach to medication review and prescribing in people who are experiencing, or are at increased risk of, delirium, and covers three broad areas:

1++

- Any changes in medications, including over the counter and herbal medications. Either commencement of new medications, changes in dosage of medication or abrupt withdrawal of medication could result in delirium.[78,79]

3

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- Changes in how the body handles and is affected by medication. The natural physiology of ageing can result in medication which has been beneficial without side effects for years, now causing or contributing to delirium. The same can also be said for acute derangements in physiology seen with illness.[78]

- Consideration of delirium risk when prescribing new medication. When assessing the risks and benefits of commencing a new medication delirium risk should be considered.[75,78]

R **All patients with delirium should have a medication review conducted by an experienced healthcare professional.**

✓ Areas with patients at high risk of delirium, such as trauma orthopaedic wards, should have protocols for commonly required medication (eg analgesia and anti-emesis) that contain choices for first-line treatments which minimise the risk of causing delirium.

5.2 MEDICAL CARE

5.2.1 ANTIPSYCHOTICS

Some, low-quality, studies suggest that prophylactic antipsychotic medication may be beneficial for the prevention of postoperative delirium in patients undergoing cardiac, general, elective joint replacements and hip fracture surgery.[80-83] One systematic review did not support its use.[84] Results in this review may have been skewed by the inclusion of a controlled trial in which an imbalance in the age of participants could have been a confounding factor. A Cochrane review concluded that there was no evidence of benefit for the use of haloperidol, but olanzapine versus placebo reduced the incidence of delirium (RR 0.36, 95% CI 0.24 to 0.52).[57]

1+

1++

There appears to be a greater benefit from antipsychotic prophylaxis the higher the baseline risk of delirium.[80] If delirium did occur, prophylaxis did not reduce the severity or duration, length of hospital stay or mortality.[80]

1++

No optimal regime for perioperative use was determined from the studies.

There is insufficient evidence to determine whether antipsychotic prophylaxis is effective in other hospital inpatients.[84-87] One study of the use of prophylactic haloperidol did not reduce incidence of delirium but was associated with a reduction in delirium duration and severity.[85]

1++
1+
1-

No adverse effects were noted, but this could be due to lack of reporting in the studies included in the systematic reviews. Common side effects include constipation, movement disorders, QTc prolongation, lower seizure threshold, urinary retention and neuroleptic malignant syndrome.[9] No antipsychotics are licensed for the prophylaxis of delirium.

There is insufficient evidence of benefit to recommend the use of antipsychotic prophylaxis in patients at risk of developing delirium after surgery.

5.2.2 SEDATION

Three studies on the use of ketamine to reduce the risk of delirium in patients undergoing surgery were inconclusive. Two studies reported no reduction in postoperative delirium compared to placebo, while one small study concluded incidence may be reduced if ketamine is given prior to cardiac surgery.[88-90] There was an increase in post-operative hallucinations and nightmares with ketamine use.[88] 1++

Systematic reviews identified four RCTs on the use of melatonin to prevent delirium in medical and surgical settings.[57,91,92] Results were inconclusive. 1++ 1+ 2+

5.3 INTENSIVE CARE

5.3.1 DEXMEDETOMIDINE

Dexmedetomidine has been utilised in a peri-operative and critical care setting. A meta-analysis identified 14 small trials of medium to low quality, incorporating 3029 general and post-operative ICU patients.[93] Dexmedetomidine was compared to other therapies (propofol, midazolam or morphine) or placebo to assess reduction of the incidence of delirium, agitation and confusion. Overall, analysis was associated with a significant reduction in the incidence of delirium with dexmedetomidine versus controls, RR 0.68, 95% CI 0.49 to 0.96.[93] Another smaller systematic review incorporating some of the same trials also found benefit from use of dexmedetomidine.[94] 1+ 1++

An RCT of 90 patients undergoing non-invasive ventilation in ICU found dexmedetomidine to be superior to haloperidol or placebo (3/30 patients given dexmedetomidine developed delirium compared to 10/30 given haloperidol and 13/30 in the placebo group).[95] Subgroup analysis of a similar patient cohort further supported a benefit with dexmedetomidine, RR 0.18, 95% CI 0.03 to 1.01.[93] 1++ 1+

Three RCTs evaluated the use of peri- and post-operative dexmedetomidine in patients undergoing non-cardiac surgery, two of which found benefit in a reduction of incidence of delirium.[96-98] The largest of these was a Chinese study, involving 700 patients who were given either dexmedetomidine or placebo post-operatively on arrival in ICU. Delirium was significantly lower in the group receiving dexmedotimidine, OR 0.35, 95% CI 0.22 to 0.54.[97] A reduction of incidence of delirium was found in elderly patients undergoing joint replacement but no benefit was seen in a small RCT which measured reduction of delirium as a secondary outcome and recruited younger patients with fewer risk factors.[96,98] 1++

A Chinese meta-analysis of four small trials compared dexmedetomidine with other peri-operative medications in patients undergoing cardiac surgery. Dexmedetomidine was associated with a reduction in the incidence of post-operative delirium, RR 0.35, 95% CI 0.2 to 0.65.[99] A reduced incidence and shorter duration of delirium was also seen in an RCT of 183 patients given either dexmedetomidine or propofol on admission to ICU following cardiac surgery.[100] 1++

Bradycardia and hypotension are known side effects of dexmedetomidine, secondary to its intrinsic effects as an alpha2-receptor agonist. Compared to other sedatives or placebo, dexmedetomidine was associated with increased risk of hypotension (RR 1.08, 95% CI) and bradycardia (RR 2.23, 95% CI 1.36 to 3.67) in patients who had undergone cardiac surgery.[100] Caution should be taken when considering its use, particularly in patients with low cardiac output state, since bradycardia is relatively common. The risk of hypotension 1++

can be reduced by either omitting or using a lower-loading dose prior to starting a continuous infusion.[99]

Results of a trial on the use of dexmedetomidine in patients who are mechanically ventilated in a general ICU setting (Early Goal Directed Sedation Compared with Standard Care in Mechanically Ventilated Patients in Intensive Care (SPICE III)) are awaited.

R **Dexemedetomidine should be considered for use in patients at high risk of developing delirium and for whom there is adequate cardiovascular monitoring, such as the critical care and peri-operative setting.**

5.3.2 ANTIPSYCHOTICS

Two small studies found that haloperidol can reduce the incidence of delirium in elderly postoperative patients in ICU (*see section 5.2.1 antipsychotics in hospital care*).[86] There was insufficient evidence identified to demonstrate efficacy in general patients in ICU.[86] Only one of five studies identified found benefit compared to placebo in a non-cardiac surgical population.[87] 1++

6 Non-pharmacological treatment

Other guidelines, narrative reviews and expert opinion on the treatment of patients with established delirium focus mainly on treating the presumed causes of the delirium, and other aspects of care such as treating distress and agitation.[1,52,54,101] Few trials have been conducted testing such approaches. There is insufficient high-quality evidence to determine the efficacy of formal packages of non-pharmacological interventions in reducing the severity or duration of delirium when it does occur.[52,55] Meta-analyses did not find a significant difference in the reduction of duration of delirium with multicomponent care or comprehensive geriatric care, compared to usual care.[56,59] One RCT did not find benefit from the use of cognitive-stimulating interventions in patients with delirium superimposed on dementia.[102]

4
2++
1++

Therefore guidance on treatment of people with delirium relies on expert consensus, which advocates multicomponent interventions as basic good practice.[52,61,62] In Scotland a comprehensive pathway, incorporating the "Triggers, Investigate, Manage, Engage" (TIME) bundle, which covers the first two hours of care, and the Scottish Delirium Association (SDA) delirium management pathway provide protocols for good care (*see Annexes 3 and 4*). NICE recommends treating the causes, effectively communicating with the patient, providing a suitable care environment, and specifically addressing distress.[52]

4

R **Healthcare professionals should follow established pathways of good care to manage patients with delirium:**

- **First consider acute, life-threatening causes of delirium, including low oxygen, low blood pressure, low glucose, and drug intoxication.**
- **Systematically identify and treat potential causes** (drug, acute illness, etc)**, noting that multiple causes are common.**
- **Optimise physiology, management of concurrent conditions, environment** (reduce noise)**, medications, and natural sleep, to promote brain recovery.**
- **Specifically detect, assess causes of, and treat agitation and/or distress, using non-pharmacological means only if possible.** *(See section 7 for pharmacological treatment).*
- **Communicate the diagnosis to patients and carers, and provide ongoing engagement and support.**
- **Aim to prevent complications of delirium such as immobility, falls pressure sores, dehydration, malnourishment, isolation.**
- **Monitor for recovery and consider specialist referral if not recovering.**
- **Consider follow-up** (*see Section 8*).

7 Pharmacological treatment

7.1 MEDICAL AND SURGICAL CARE

7.1.1 ANTIPSYCHOTIC THERAPIES

Studies of the efficacy of antipsychotics are heterogenous and inconclusive. Most are small and rated as low quality.[84,86,103] One meta-analysis concluded that antipsychotics should not be used in non-ICU settings for the treatment of patients with delirium, while another concluded that antipsychotics were superior to placebo or usual care in reducing delirium severity scale scores.[84,103] A further, large RCT in patients receiving palliative cancer care found that patients treated with either risperidone or haloperidol had worse delirium symptom scores than those receiving placebo.[104]

2++

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Comparisons of haloperidol and other antipsychotics did not find any drug to be more effective than another.[86,103,105] Two RCTs comparing the efficacy of haloperidol and quetiapine reported conflicting results.[103,106]

1+

2++

No serious side effects were reported in the studies of haloperidol.[86] It was associated with higher incidence of extrapyramidal side effects and dystonias than second generation antipsychotics.[103,105] This may be due to the high dose of haloperidol used in the trials. Haloperidol is contraindicated in combination with any drug that is associated with QTc prolongation.[107]

2++

2+

If commenced, the medication should be reviewed on a daily basis, stopped as soon as the clinical situation allows. Antipsychotics prescribed for delirium should be stopped as soon as the clinical situation allows, typically within 1-2 days**.** In situations where it is deemed safer to continue antipsychotic therapy for delirium beyond discharge or transfer from hospital, a clear plan for early medication review and follow-up in the community should be agreed.

7.1.2 ACETYLCHOLINESTERASE INHIBITORS

Seven small trials of either rivastigmine or donezepil found no benefit for reducing the duration of delirium or length of hospital stay compared to placebo or haloperidol in patients in surgical or medical settings.[108] Four of the seven studies found acetylcholinesterase inhibitors to have similar tolerability to placebo.[108] *See section 7.2.2 for evidence for acetylcholinesterase inhibitors in patients in ICU.*

1+

7.1.3 BENZODIAZEPINES

Only one small trial (n=30) on the use of lorazepam in the treatment of patients with delirium. The trial, in patients with AIDs in a hospital setting, found no benefit from lorazepam and treatment was stopped early due to intolerable side effects.[105]

2+

7.2 INTENSIVE CARE

7.2.1 ANTIPSYCHOTICS

Pooled subgroup analysis of two small trials of patients in ICU with delirium found use of antipsychotics to be marginally superior to placebo in response rate at the studies' endpoint (risk ratio 0.25, 95% CI 0.06 to 1.02). Second generation antipsychotics were superior to haloperidol in reducing delirium severity scores in patients in ICU (standardised mean difference (SMD) -0.52, 95% CI -0.85 to -0.19). There was no difference in discontinuation rates or adverse events.[103]

1++

A systematic review identified five studies, one of which reported that quetiapine reduced the duration of delirium (1 day versus 4.5 days) compared to placebo, in 36 patients.[87] None of the studies reported a reduction in length of stay, or mortality. 1+

Because the studies identified are underpowered, further, larger trials are needed before recommendations can be made on the use of antipsychotics for the treatment of patients in ICU with delirium.

7.2.2 ACETYLCHOLINESTERASE INHIBITORS

A systematic review identified one RCT (104 participants) which reported longer duration of delirium and longer length of hospital stay in patients with delirium in ICU given a combination of haloperidol and rivastigmine compared to those given haloperidol and placebo.[108] There were three times as many deaths among patients receiving the haloperidol and rivastigmine combination.[108] There is insufficient evidence to draw conclusions on the efficacy and safety of the use of acetylcholinesterase inhibitors for the treatment of patients with delirium. 1+

7.2.3 DEXMEDETOMIDINE

A small RCT on the use of dexmedetomidine in patients with agitated delirium receiving mechanical ventilation in ICU reported secondary outcomes of a reduction in delirium (23.3 hours versus 40 hours with placebo) and reduced the length of ICU stay.[109] 1+

7.3 ROLE OF MEDICATION IN SPECIFIC SITUATIONS

While the evidence for pharmacological treatment is insufficient to support a recommendation, expert opinion supports a role for medication in specific situations such as in patients in intractable distress, and where the safety of the patient and others is compromised (*see Annex 4*).

8 Follow up

Older patients who develop delirium may have undiagnosed underlying dementia or mild cognitive impairment.[110,111] Delirium is also associated with an increased rate of cognitive decline post-delirium.[110,111] The majority of studies identified found that delirium is a risk factor for future cognitive decline.[112-115] Longer duration of delirium has been linked to worse global cognition at three and 12 months follow up.[113] 3 2++

A systematic review of non-comparative prospective studies concluded that people may develop depression after experiencing delirium.[116] The length of time before people experience depression post-delirium in ICU varied between studies, with some reporting no association between delirium and depression at three months, but higher rates of depression and worse mental health status at 12 months, and others reporting depression at three, four, six and 12 months.[116,117] Other studies did not find a significant association between delirium, post-traumatic stress disorder (PTSD), anxiety or depression.[118-120] In these studies the patient groups were younger (mean ages 42, 61 and 62 compared to mean age >80 years in the majority of studies in the systematic review).[116,118-120] 2+ 3

The studies addressed a variety of population groups, in acute and ICU settings, and used different measures for delirium, mental and cognitive impairment and depression.

R **Healthcare professionals should be aware that older people may have pre-existing cognitive impairment which may have been undetected, or exacerbated in the context of delirium. Appropriate cognitive assessment should be considered. Timing of this assessment must take into account persistent delirium.**

R **In patients who have experienced delirium in ICU consideration should be given to follow up for psychological sequelae including cognitive impairment.**

✓ Patient records should be coded to highlight a previous episode of delirium so that hospital staff are aware of the increased risk on readmission.

✓ Ensure that delirium is noted in the discharge letter for general practitioners.

9 Provision of information

This section reflects the issues likely to be of most concern to patients and their carers. These points are provided for use by health professionals when discussing delirium with patients and carers and in guiding the production of locally produced information materials.

9.1 SOURCES OF FURTHER INFORMATION

Scottish Delirium Association
www.scottishdeliriumassociation.com
The Scottish Delirium Association consists of healthcare professionals working to share best practice in delirium by providing education, promoting research and raising awareness of the condition.

Critical Care Recovery
www.criticalcarerecovery.com
A website developed by the NHS to offer information, advice and support on recovery after intensive care.

Patient information leaflets:

THINK Delirium
www.knowledge.scot.nhs.uk/media/CLT/ResourceUploads/4052742/20141007%20Delirium%20leaflet%20(web).pdf
Patient information leaflet developed by Healthcare Improvement Scotland in collaboration with NHS boards.

www.alzheimers.org.uk/info/20029/daily_living/370/delirium

www.dementiauk.org/delirium/

www.mariecurie.org.uk/professionals/palliative-care-knowledge-zone/symptom-control/delirium

www.nhs.uk/conditions/confusion/

cks.nice.org.uk/delirium

www.rcpsych.ac.uk/healthadvice/problemsanddisorders/delirium.aspx

Telephone helplines:

Alzheimers Scotland
0808 808 3000
helpline@alzscot.org

DementiaUK
Tel: 0800 888 6678

9.2 CHECKLIST FOR PROVISION OF INFORMATION

This section gives examples of the information patients/carers may find helpful at the key stages of the patient journey. The checklist was designed by members of the guideline development group based on their experience and their understanding of the evidence base. The checklist is neither exhaustive nor exclusive.

If patients are at risk of delirium

Identify the family and/or main carer of the patient.

- Ensure that their contact details are on file. If the patient lacks capacity, ascertain whether a family member or carer has Power of Attorney/Guardianship over welfare.

Explain to the patient and the family/carer about delirium:

- Delirium is common amongst hospitalised patients especially following an operation.

- Acute triggers of delirium include:
  - infection, dehydration, severe constipation, urinary retention, and pain
  - critical illness
  - surgery especially heart and hip operations
  - side effects of new drugs or drug withdrawal

- Those most at risk are:
  - older people
  - older people on multiple medicines
  - people with dementia, Parkinson's disease or stroke
  - people who are hearing or visually impaired.

Ask family/carers to alert medical staff if they notice any change to their relative's normal behaviour.

If a patient develops delirium

Explain to the family/carers that delirium is mental confusion that often starts suddenly but usually improves when the physical condition improves and the underlying cause gets better.

Discuss treatment options and possible side effects with the patient and/or carer.

Provide the family/carer with appropriate information leaflets.

It is important for carers and relatives to participate and work together with the clinical team in hospital or home to clear delirium and see the affected person back to good health.

Explain that the person affected with delirium may show many different types of change. They may:

- be less aware of their surroundings
- be unable to speak clearly or follow conversations
- have dreams which can sometimes be frightening and can carry on when they wake up
- hear voices or noises which may not be present (auditory hallucinations)
- see objects or people that are not present or in different context (visual hallucinations)
- get upset that other people are trying to harm them
- be agitated or restless and wander about, unable to sit still
- be sleepy and slow to move and respond

- have all or some of the above and that could quickly change
- have worse symptoms in the evenings or overnight.

Let the family/carer know how to help someone with delirium:

They can help by reassuring and reorienting the patient, eg:

- ensure they have their hearing aids, glasses and dentures available at all times
- have a gentle and friendly approach, smiling and providing reassurance
- talk to them and keep them informed in short, simple sentences
- check that they have understood you and be prepared to repeat if necessary
- familiarity helps, so try to make sure that someone they know well is with them
- try not to agree with any incorrect ideas but disagree with tact and change the subject
- keep a calendar and/or clock with in their view and remind them of the surroundings
- bring in some familiar objects from home to the hospital to keep next to their bed side
- remind them and assist if required to eat and drink.

The key is to remain calm and help the affected person feel calm and in control.

At discharge following an acute episode of delirium

Liaise with the family/carers regarding discharge arrangements. Discuss with family/carers whether they need extra support. Some patients may still be a little confused, not entirely themselves or less able than usual to carry out their daily activities.

Inform carers of their right to have a new or updated adult carer support plan.

Ensure that support is in place before the patient is discharged to their home.

If there are concerns about cognitive impairment in the following months, advise to see their general practitioner (GP).

10 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

10.1 IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Implementation of this guideline will be encouraged and supported by SIGN. The implementation strategy for this guideline encompasses the following tools and activities.

10.2 RESOURCE IMPLICATIONS OF KEY RECOMMENDATIONS

No recommendations are considered likely to reach the £5 million threshold which warrants resource impact analysis.

10.3 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

Quality of care for older patients with delirium can be measured against the Healthcare Improvement Scotland Care of Older People in Hospital standards.[121]

To assist with the implementation of this guideline the guideline development group has identified the following as key points to audit:

The percentage of:

- at risk patients assessed using the 4AT tool
- critically ill patients assessed using CAM-ICU or ICDSC (take account of appropriate sedation level)
- patients with confirmed delirium who are recorded and coded with delirium, and the diagnosis is included in discharge summaries to the GP
- patients who have medication review and medications stopped as a result
- patients followed up by GP after delirium
- compliance with depth of anaesthesia monitoring.

10.4 HEALTH TECHNOLOGY ASSESSMENT ADVICE FOR NHSSCOTLAND

In May 2012 the SMC accepted dexmedetomidine hydrochloride for sedation in adult intensive care unit patients requiring a sedation level not deeper than arousal in response to verbal stimulation (corresponding to RASS 0 to -3).

11 The evidence base

11.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Evidence and Information Scientist. Databases searched include Medline, Embase, Cinahl, PsycINFO and the Cochrane Library. The year range covered was 2012–2017. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two Evidence and Information Scientists using standard SIGN methodological checklists before conclusions were considered as evidence by the guideline development group.

The search strategies are available on the SIGN website, www.sign.ac.uk

11.1.1 LITERATURE SEARCH FOR PATIENT AND CARER ISSUES OR CONCERNS

At the start of the guideline development process, a SIGN Evidence and Information Scientist conducted a literature search for qualitative and quantitative studies that addressed patient and carer issues of relevance to patients with delirium and their carers. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised by the SIGN Patient Involvement Officer and presented to the guideline development group.

11.1.2 LITERATURE SEARCH FOR COST-EFFECTIVENESS EVIDENCE

The guideline development group identified key questions with potential cost-effectiveness implications, based on the following criteria, where it was judged particularly important to gain an understanding of the additional costs and benefits of different treatment strategies:

- treatments which may have a significant resource impact
- opportunities for significant disinvestment or resource release
- the potential need for significant service redesign
- cost-effectiveness evidence could aid implementation of a recommendation.

A systematic literature search for economic evidence for these questions was carried out by a SIGN Evidence and Information Scientist covering the years 2012–2017. Databases searched include Medline, Embase and NHS Economic Evaluation Database (NHS EED). Each of the selected papers was evaluated by a Health Economist, and considered for clinical relevance by guideline group members.

Interventions are considered to be cost effective if they fall below the commonly-accepted UK threshold of £20,000 per Quality-Adjusted Life Year (QALY).

11.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline (*see Annex 1).* The following areas for further research have been identified:

- Validation of tools for routine monitoring of patients with delirium with clarification of the frequency of using these tools and their impact on outcomes and cost effectiveness.
- Studies of the practicalities and diagnostic yield of performing EEG in adults presenting with delirium.
- RCTs on the efficacy of depth of anaesthesia monitoring in reducing postoperative delirium in patients with dementia undergoing surgery and patients undergoing emergency surgery or trauma orthopaedic surgery.

- Trials of multicomponent interventions for the treatment of patients with delirium in general hospital settings.
- Large multi-centre trial detailing a package of non-pharmacological interventions in the ICU with evidence of implementation.
- RCTs on the efficacy and safety of antipsychotics to reduce the risk of delirium in patients in ICU or other hospital settings.
- RCTs on the efficacy and safety of haloperidol in the reduction in severity and duration of delirium in non-ICU settings.
- RCTs on the efficacy and safety of antipsychotics, benzodiazepines or dexmedetomidine in the reduction of severity and duration of delirium in patients in ICU.

11.3 REVIEW AND UPDATING

This guideline was issued in 2019 and will be considered for review in three years. The review history, and any updates to the guideline in the interim period, will be noted in the review report, which is available in the supporting material section for this guideline on the SIGN website: **www.sign.ac.uk**

Comments on new evidence that would update this guideline are welcome and should be sent to the SIGN Executive, Gyle Square, 1 South Gyle Crescent, Edinburgh, EH12 9EB (email: sign@sign.ac.uk).

12 Development of the guideline

12.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising healthcare professionals using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at **www.sign.ac.uk**

This guideline was developed according to the 2015 edition of SIGN 50.

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The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest. A register of interests is available in the supporting material section for this guideline at **www.sign.ac.uk**

Guideline development and literature review expertise, support and facilitation were provided by SIGN Executive and Healthcare Improvement Scotland staff. All members of the SIGN Executive make yearly declarations of interest. A register of interests is available on the contacts page of the SIGN website **www.sign.ac.uk**

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12.3 ACKNOWLEDGEMENTS

SIGN is grateful to the following former members of the guideline development group and others who have contributed to the development of the guideline.

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Mr James McKillop	*Patient representative, Glasgow*
Ms Rachael Wybrew	*Medical student, Birmingham*

12.4 CONSULTATION AND PEER REVIEW

12.4.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 21 June 2018 and was attended by XX representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

12.4.2 SPECIALIST REVIEWERS INVITED TO COMMENT ON THIS DRAFT

This guideline was reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments. A report of the peer review comments and responses is available in the supporting material section for this guideline on the SIGN website. All expert referees made declarations of interest and further details of these are available on request from the SIGN Executive.

SIGN is very grateful to all of these experts for their contribution to the guideline.

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12.4.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council Membership page of the SIGN website **www.sign.ac.uk**

Dr Roberta James	*SIGN Programme Lead; Co-Editor*
Professor John Kinsella	*Chair of SIGN; Co-Editor*

Abbreviations

4AT	4 A's Test
AMT	Abbreviated Mental Test
CAM	Confusion Assessment Method
CI	confidence interval
CRP	c-reactive protein
CSF	cerebrospinal fluid
CT	computed tomography
CXR	chest x-ray
DOS	Delirium Observation Screening Scale
DRS-98-R	Delirium Rating Scale
DSD	delirium superimposed on dementia
ECG	electrocardiogram
EEG	electroencephalogram
FBC	full blood count
GMC	General Medical Council
GP	General practitioner
ICU	intensive care unit
ICDSC	Intensive Care Delirium Screening Checklist
LFT	liver function test
MA	marketing authorisation
MMSE	Mini Mental State Examination
NCSE	non-convulsive status epilepticus
NICE	National Institute for Health and Care Excellence
Nu-DESC	Nursing Delirium Scale
OR	odds ratio
PCR	polymerase chain reaction
PTSD	post-traumatic stress disorder
QALY	quality-adjusted life year
RADAR	Recognising acute delirium as part of your routine
RASS	Richmond Agitation-Sedation Scale
RCT	randomised controlled trial
RR	relative risk
SDA	Scottish Delirium Association
SIGN	Scottish Intercollegiate Guidelines Network
SMC	Scottish Medicines Consortium
SQiD	Single Question to Identify Delirium

TCD	transcranial doppler
TIME	Triggers, Investigate, Manage, Engage
UTI	urinary tract infection

Annex 1
Key questions used to develop the guideline

This guideline is based on a series of structured key questions that define the target population, the intervention, diagnostic test, or exposure under investigation, the comparison(s) used and the outcomes used to measure efficacy, effectiveness, or risk. These questions form the basis of the systematic literature search.

Guideline section	Key question

1. What tool(s) should be used to detect delirium and when?

   Population: Adults at risk of delirium
   Interventions:
   Assessment tools:
   a. 4AT
   b. Confusion Assessment Method Instrument (CAM)
   c. 3D CAM
   d. Delirium Observation Screening Scale
   e. Single Question to Identify Delirium (SQID)
   f. Memorial Delirium Assessment Scale (MDAS)
   g. Recognizing acute delirium as part of your routine (RADAR)
   h. Delirium Rating Scale (DRS-R98)
   i. Intensive Care Delirium Screening Checklist (ICD-SC)
   j. CAM-ICU
   k. RASS/Modified RASS
   l. Family CAM (FAM-CAM)
   m. Brief CAM (B-CAM)
   n. NU desk
   o. Organic Brain Syndrome (OBS) scale
   p. MMSE

   Comparison: Diagnostic and Statistical Manual (DSM 5) or International Classification of Diseases (ICD-10) defined diagnosis; between tools

   Outcomes: Sensitivity, specificity, evidence of adherence in clinical practical

2. What tool(s) should be used for monitoring purposes and when should they be used?

   Population: Adults at risk of delirium
   Interventions:
   Monitoring tools:
   a. Modified RASS (Richmond agitation sedation score)
   b. 4AT
   c. Confusion Assessment Method Instrument (CAM)
   d. 3D CAM
   e. Delirium Observation Screening Scale
   f. Single Question to Identify Delirium (SQID)
   g. Memorial Delirium Assessment Scale (MDAS)
   h. Recognizing acute delirium as part of your routine (RADAR)
   i. Delirium Rating Scale (DRS-R98)
   j. Intensive Care Delirium Screening Checklist (ICD-SC)
   k. CAM-ICU
   l. FAM-CAM
   m. B-CAM
   n. NU desk delirium screening

o. Organic Brain Syndrome (OBS) scale

Comparison: Diagnostic and Statistical Manual (DSM 5) or International Classification of Diseases (ICD-10) defined diagnosis; between tools

Outcomes: Sensitivity, specificity, evidence of adherence in clinical practical

3. What (other) investigations are useful when assessing a patient for delirium?

   Population: Adults with suspected delirium
   Intervention:
   a. imaging (CT or MRI scans)
   b. lumbar puncture
   c. electroencephalogram (EEG)
   d. testing for antibodies for autoimmune encephalitis
   e. toxicology screening

   Comparison: Usual care
   Outcomes: Sensitivity, specificity, cost effectiveness

4. What risk reduction strategies for patients at risk of delirium are effective?

   Population: Patients at risk of developing delirium
   Interventions:
   Multicomponent interventions – non-pharmacological and pharmacological
   Non-pharmacological:
   a. proactive screening of delirium and pre-existing cognitive impairment including dementia
   b. hydration
   c. catheterization avoidance
   d. sensory impairment
   e. constipation
   f. sleep hygiene and promotion
   g. falls prevention and mobility
   h. providing means of communication
   i. impact of ward moves (incl “boarding”)
   j. environmental factors

   Pharmacological:
   a. medication reconciliation
   b. pain relief
   c. antipsychotics and benzodiazepines (medical and surgical patients)
   d. sedation for night-time sleep

   Comparison: usual care
   Outcomes: Incidence of delirium (hospital acquired), prevalence of delirium (community acquired), duration of delirium, severity of delirium

5. What are the most effective non-pharmacological strategies for managing patients with delirium?

   Population: people with delirium
   Interventions:
   Multicomponent non-pharmacological interventions

   (Staff) behavioural adaptations:
   - calm non-confrontational manner
   - reassurance
   - reorientation
   - distraction/de-escalation techniques
   - one-to-one nursing
   - cognitive stimulation

Environmental adaptations:

- single room
- well lit area
- clear signs re: day, time, season, place
- familiar objects
- family input
- minimise bed moves
- activities and OT
- address sensory impairment
- sleep promotion
- facilitate mobility

Address specific causes of stress:

- pain
- hunger
- feeling too hot/too cold
- thirst/dry mouth
- urinary retention
- specific fears
- not understanding what is happening
- hallucinations, delusions, aggression, agitation, and wandering/searching

Comparison: Usual care, pharmacological therapies
Outcomes: Mortality, complete response, duration of delirium, severity of delirium, distress in delirium, length of hospital stay, loss of independent living /new institutionalisation, reduction in depression and anxiety, reduced dementia risk, worsening of dementia, reduction in long-term effects, reduction in falls, cost effectiveness

6. What are the most effective pharmacological strategies for managing patients with delirium?

   Population: Patients with delirium
   Consider hyperactive versus hypoactive delirium.
   Consider sub-populations:
   1. Parkinson's disease
   2. delirium superimposed on dementia
   3. patients already taking long-term medication

   Interventions:
   a. antipsychotics
   b. benzodiazepines
   c. acetylcholinesterase inhibitors
   d. melatonin
   e. antidepressants
   f. dexmedetomidine
   g. clonidine
   h. propanolol
   i. withdrawal of culprit drugs

   Comparison: Usual care, between therapies
   Outcomes: Mortality, complete response, duration of delirium, severity of delirium, length of hospital stay, loss of independent living/new institutionalisation, increased dementia risk, worsening of dementia, adverse events, reduction in long-term effects, cost effectiveness

7. What follow-up care should patients receive after experiencing delirium?

   Population: patients who have had delirium

Interventions:
Screening for:

a. dementia
b. functional psychiatry disorders – post traumatic stress disorder, depression

Comparison: usual care
Outcomes: incidence of dementia post delirium, incidence of psychiatric disorders

Annex 2
Investigations for underlying causes of delirium

The majority of people with delirium are older adults, often with a vulnerability to delirium due to underlying neurological disease (eg dementia, cerebrovascular disease, Parkinson's Disease). In each there is commonly more than one precipitating factor. Identifying these factors and addressing those that are modifiable underpin the treatment of a person with delirium.

A good clinical history taking into account premorbid illness, cognition and level of function gives key information. However, in delirium the person may not be able to provide reliable information themselves due to confusion or diminished attentiveness. A collateral history from the person's family or carers should be obtained to confirm and supplement information provided by the person. This collateral history should be sought at the earliest opportunity. Relatives will often accompany the unwell person when initially assessed in hospital or at home. Some additional time obtaining this information at an early stage can assist rapid identification and treatment of precipitants.

A full clinical examination should be undertaken including neurological examination to identify focal signs and musculoskeletal examination to look for evidence of injury. Confusion and agitation resulting in poor co-operation or understanding of instructions may make examination difficult.

Severe illness should be identified and rapidly treated as an urgent priority (*see TIME bundle in Annex 3*). This should include assessment of basic observations, blood oxygen saturations, and blood glucose with near-patient testing to exclude hypoglycaemia. Drug intoxication should be considered in every case.

The information obtained from history and investigation will guide further investigation – some would be considered general and applicable to most patients, while others are targeted to specific clues from history and examination. Investigations will also depend on the setting, whether the person is in hospital or at home.

These tests are commonly done but this list is not entirely comprehensive.

Blood tests:

- Renal function (urea & electrolytes) – identify dehydration, acute kidney injury, chronic kidney disease, hyponatraemia.
- Full blood count (FBC) – identify anaemia, macrocystosis, elevated white cell count
- C-reactive protein (CRP) – identify inflammation/infection
- Liver function tests (LFT) – can identify liver dysfunction which could identify biliary infection, malignant disease, encephalopathy
- Calcium – hypercalcaemia can cause confusion, and requires further investigation
- Blood cultures – where there is evidence of infection (eg fever or sepsis)
- Thyroid function – thyroid dysfunction can cause confusion
- Vitamin B12 and Folate - consider if concerns about nutrition or macrocytosis on full blood count.

Electrocardiogram (ECG)

- this may identify clinically silent myocardial ischaemic or arrhythmia which may be significant (such as atrial fibrillation).

Radiological imaging

- Chest x-ray (CXR) – should be done if symptoms or signs of chest pathology such as infection. It should be remembered that clinical examination may not reveal all pathology, such as tumour, and should be considered.
- Musculoskeletal x-rays – target where evidence of injury or suspicion of fracture.
- Other imaging should be guided by history, examination and initial investigations.

Other basic tests

- Identify hypoxia using pulse oximetry
- Urine dipstick and culture – a negative urine dipstick can be useful, in that urinary tract infection (UTI) would be very unlikely, but a "positive" dipstick does not necessarily mean infection. Asymptomatic bacteruria can also exist in the elderly and delirium may mean that the person is unable to give a history of symptoms of UTI. This may cloud the situation and treatment of suspected urinary tract infection should be based on clinical grounds and probability.
- Bedside ultrasound bladder scan – to identify urinary retention

This is not a comprehensive list of tests which could be done and investigation should be targeted from information obtained initially and built on as the clinical situation evolves. Section 3 addresses investigations where an evidence base was found.

Where there is consideration of central nervous system pathology as a cause of confusion or delirium, targeted investigations may be appropriate including brain imaging, lumbar puncture, EEG, auto-antibody testing (such as for auto-immune encephalitis – anti voltage-gated potassium channel antibodies, anti-NMDA antibodies).

Annex 3
TIME bundle delirium management protocol[62]

TIME bundle

Name:
Date of birth:
CHI number:

Date: / /
Zero time: :

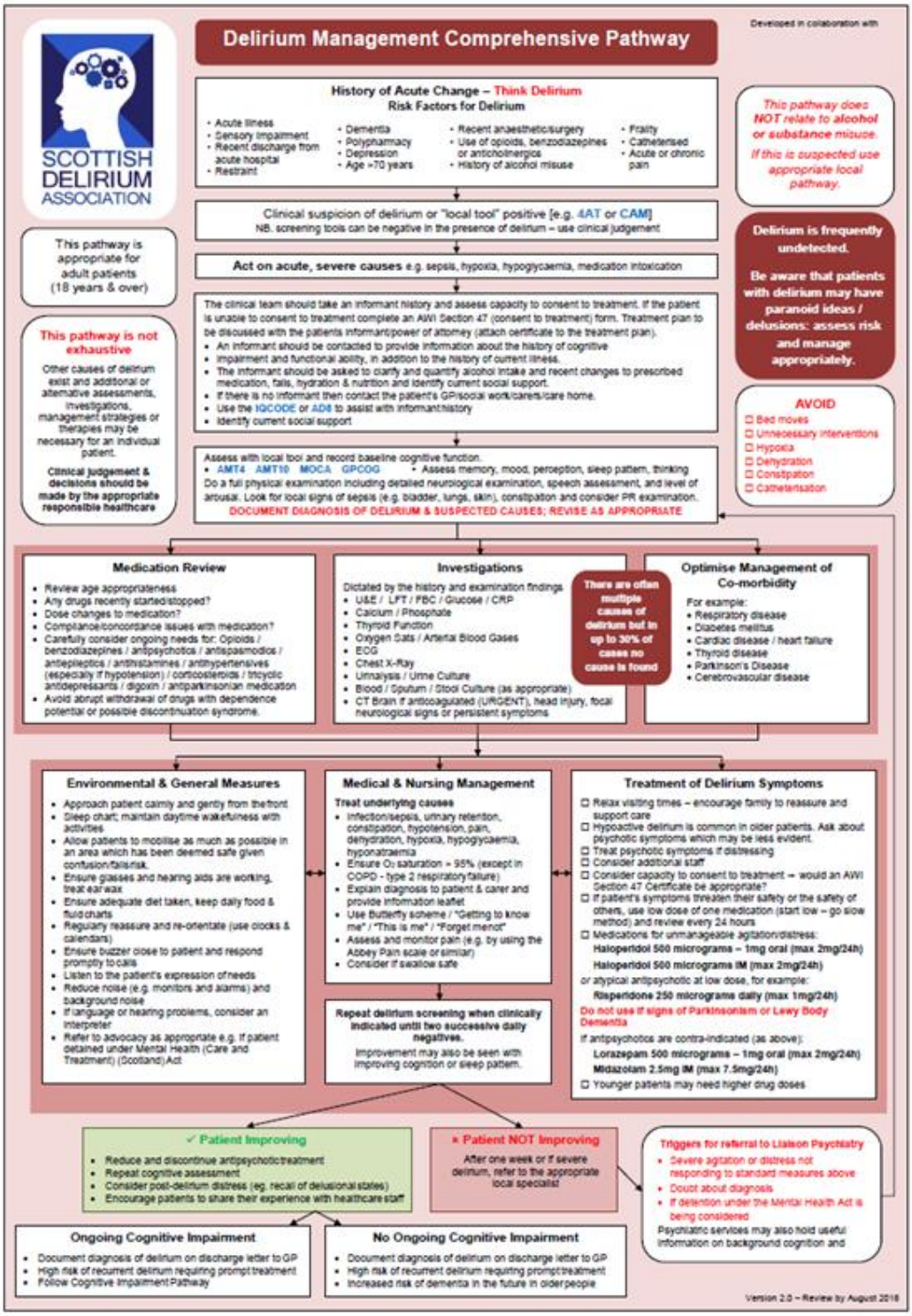
Practitioner name: _____ **Practitioner signature:** _____

Designation: _____

	Initiate TIME within 2 hours (initial and write time of completion)	**Assessed/ sent**	**Results seen**	**Abnormality found**
	Think exclude and treat possible triggers			
	NEWS (think sepsis six)			
	Blood glucose			
T	Medication history (identify new medications/change of dose/medication recently stopped)			
	Pain review (Abbey Pain Scale)			
	Assess for urinary retention			
	Assess for constipation			
	Investigate and intervene to correct underlying causes			
	Assess Hydration and start fluid balance chart			
	Bloods (FBC, U&E, Ca, LFTs, CRP, Mg, Glucose)			
I	Look for symptoms/signs of infection (skin, chest, urine, CNS) and perform appropriate cultures/imaging depending on clinical assessment (see sepsis six)			
	ECG (ACS)			
M	**Management Plan**			***Completed***
	Initiate treatment of ALL underlying causes found above			
	Engage and Explore (complete within 2 hours or if family/carer not present within 24 hours)			
E	Engage with patient/family/carer – explore if this is usual behaviour. Ask: How would you like to be involved?			
	Explain diagnosis of delirium to patient and family/carers (use delirium leaflet)			
	Document diagnosis of delirium			

v3.0 Testing May 2014

Annex 4
Scottish Delirium Association delirium management pathway[62]



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